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COMPLETE SPECIFICATION

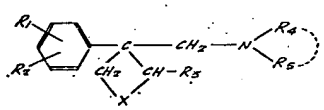
Phenyl-Cycloalkane-Methylamines and processes of preparing them

FARH

We, FARBWERKE HOECHST AKTIENGESELLSCHAFT vormals Meister Lucius & Brüning, a body corporate recognised under German law, of Frankfurt (M) - Hoechst, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with new phenyl - cycloalkane - methylamines, processes for their manufacture and their use.

The present invention provides phenyl - cycloalkane - methyl amines of the formula



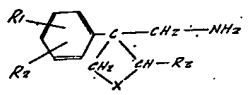
(I),

in which R_1 and R_2 each represents a hydrogen atom or a hydroxy, methyl or methoxy group, or together represent a methylene - dioxy group, X together with the CH_2 and CHR_3 groups and the adjacent carbon atom represent a cycloalkane ring containing 3 to 5 carbon atoms, R_3 represents a hydrogen atom or an alkyl group containing 1 to 3 carbon atoms, R_4 and R_5 each represents a hydrogen atom, a saturated or unsaturated aliphatic hydrocarbon group containing up to 4 carbon atoms or a cycloalkyl group containing 4 to 6 carbon atoms or together with the nitrogen atom represent a saturated ring which may be interrupted by a further hetero atom, and acid addition salts of these compounds.

The present invention also provides pharmaceutical preparations comprising the new phenyl - cycloalkane - methyl - amines or their physiologically tolerable acid addition salts in admixture or conjunction with a pharmaceutically suitable carrier.

The present invention further provides processes for the preparation of phenyl - cycloalkane - methylamines of the formula I according to methods which are generally used for the preparation of such compounds.

The new compounds may be obtained, for example, by a) reacting amines of the formula II



(II),

in which R_1, R_2, R_3 and X have the meanings given above, with esters of the formula III

$$Y—R_4 \qquad \text{(III)},$$

in which R_4 has the meaning given above and Y represents the residue of an inorganic or organic acid or

b) reducing amines of the formula II in the presence of oxo - compounds of the formula IV

$$OC\!<^{R_6}_{R_7} \qquad \text{(IV)},$$

in which R_6 and R_7 each represents a hydrogen atom or a saturated or unsaturated aliphatic hydrocarbon group containing up to 3 carbon atoms, or

c) heating amines of the formula II in the presence of alcohols of the formula V

$$HO—R_4 \qquad \text{(V)},$$

[*Price 4s. 6d.*]

in which R_5 represents an alkyl group containing 1 to 4 carbon atoms, in the presence of a large amount of Raney nickel, or

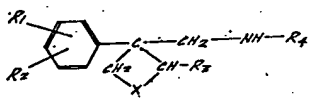
d) reacting amines of the formula II with compounds of the formula VI

$$\begin{matrix}\text{Hal}\\ \text{Hal}\end{matrix}\!>\!(CH_2)_n \qquad \text{(VI)},$$

in which n represents an integer from 3 to 5 and "Hal" represents a halogen atom, preferably chlorine or bromine, advantageously in the presence of agents splitting off hydrogen halide, or

e) reacting amines of the formula II with benzaldehyde, adding to the benzylidene compounds so obtained esters of the formula III and splitting off the acid radial from the resulting addition products by means of hydrolysis, or

f) reacting amines of the formula VII



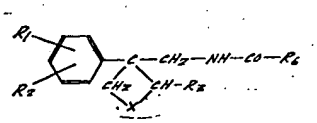
(VII),

in which R_1 to R_4 and X have the meanings given above, with esters of the formula VIII

$$Y\text{—}R_5 \qquad \text{(VIII)},$$

in which R_5 and Y have the meanings given above, or

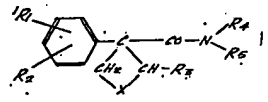
g) reducing amides of the formula IX



(IX),

in which R_1 to R_3, R_6 and X have the meanings given above, with lithium - aluminium - hydride, or

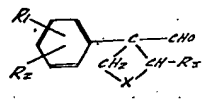
h) reducing amides of the formula X



(X),

in which R_1 to R_5 and X have the meanings given above, with lithium - aluminium - hydride, or

i) reducing aldehydes of the formula XI



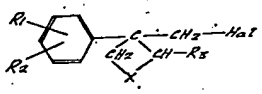
(XI),

in which R_1 to R_3 and X have the meanings given above, in the presence of amines of the formula XII

$$HN\!<\!\begin{matrix}R_4\\ R_5\end{matrix} \qquad \text{(XII)},$$

in which R_4 and R_5 have the meanings given above, or

j) reacting compounds of the formula XIII



(XIII),

in which R_1 to R_3 and X have the meanings given above and "Hal" represents a halogen atom, preferably bromine, with amines of the formula XII, or

k) demethylating the methoxy groups in compounds of the formula I in which R_1 and/or R_2 represent methoxy group(s).

The new products are valuable medicaments possessing, in particular, central-analeptic properties.

Referring to the general formula I of the new compounds of the invention, the atoms or groups represented by R_1 and R_2 may be the same or different. R_1, for example, may represent a hydrogen atom, while R_2 represents a hydroxy group, or a methyl or methoxy group. Furthermore, both the symbols R_1 and R_2 together may, for example, represent a methylene-dioxy group. Their position in the benzene nucleus may vary so that, it is possible, for example, to have a substituent in the ortho, meta or para position or two substituents in different positions.

The atoms or groups represented by R_4 and R_5 may also be identical or different. As saturated or unsaturated aliphatic hydrocarbon groups represented by R_4 and R_5 there may be mentioned, for example: methyl, ethyl, isopropyl, n - butyl, isobutyl, sec.-butyl and allyl; as cycloalkyl groups represented by R_4 or R_5 there may be mentioned the cyclopentyl and cyclohexyl groups. Both the symbols R_4 and R_5 together with the nitrogen atom may also represent a saturated ring system that may be interrupted by a further hetero atom, for

example nitrogen, oxygen or sulphur. As examples of such ring systems there may be mentioned: azetidine, methylazetidine, pyrrolidine, dimethyl - pyrrolidine, piperidine, hexamethylene - imine, morpholine, thiamorpholine and piperazine.

The symbol R_3 represents a hydrogen atom or an alkyl group containing 1 to 3 carbon atoms, for example methyl, ethyl or *n* - propyl. The cycloalkane ring formed by the central carbon atom, the CH_2 and CHR_3 groups and the radical represented by X may be for example: cyclopropane, methyl - cyclopropane, ethyl - cyclopropane, cyclobutane, methyl - cyclobutane and cyclopentane.

As amines of the formula II there may be mentioned, for example:

1 - phenyl - aminomethyl - cyclopropane,
1 - phenyl - 1 - aminomethyl - methylcyclopropane,
1 - phenyl - 1 - aminomethyl - cyclobutane,
1 - (3^1 - methoxy - phenyl) - 1 - aminomethyl-cyclobutane,
1 - (4^1 - methyl - phenyl) - 1 - aminomethyl - cyclobutane,
1 - (3^1,4^1 - dimethoxy - phenyl) - 1 - aminomethyl - cyclobutane,
1 - (2^1,4^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclobutane,
1 - phenyl - 1 - aminomethyl - cyclopentane,
1 - (2^1 - methyl - phenyl) - 1 - aminomethyl - cyclopentane,
1 - (3^1 - methoxy - phenyl) - 1 - aminomethyl-cyclopentane,
1 - (3^1,4^1 - methylene - dioxy - phenyl) - 1 - aminomethyl - cyclopentane,
1 - (2^1,4^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane,
1 - (2^1,5^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane, and
1 - (3^1,4^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane.

The starting materials are advantageously obtained by the catalytic hydrogenation of the corresponding nitriles which, for their part, can be prepared by the reaction of correspondingly substituted benzylcyanides with twice the molar amount of sodium amide and the equimolar amount of a dihalogen - alkane in an organic solvent immiscibile with water, at temperatures between 20 and 80°C.

As esters of the general formula III there may be used, for example a hydrohalic acid or sulphonic acid ester of aliphatic alcohols. The reaction of the amines of the formula II and the esters of the formula III is advantageously performed by heating the reactants in an appropriate solvent such as ethanol, benzene, toluene or xylene at temperatures between 80 and 130°C. The heating period depends upon the temperature and the reactivity of the ester used and amounts in general to 2 to 20 hours. In order to bind the hydrohalic acid or the sulphonic acid set free in the course of the reaction, an excess amount of the amine used is advantageously employed. During the reaction the corresponding amine salt is formed which, in general, is obtained in a crystalline form and which may be separated off after cooling of the reaction mixture in the usual manner, for example by applying suction or shaking the reaction solution with water, whereupon the desired reaction product can be isolated in the form of a salt by distilling off the solvent or by extracting the solvent with acids. Instead of the amine of formula II there can, however, also be used other basic compounds, for example sodium bicarbonate, sodium carbonate or tertiary amines such as triethylamine or dimethylaniline, for binding the acid set free.

When operating with sodium carbonate or sodium bicarbonate the reaction is preferably carried out while thoroughly stirring in a solvent immiscible with water and after the heating has been terminated the sodium salt that has formed is eliminated, whereupon the reaction products can be further worked up according to the method described above. When using tertiary amines for binding the acids formed it is also possible to operate with solvents miscible with water, such as, for example, ethanol. For the further treatment the solvent is, in this case, advantageously distilled off and the residue is dissolved in water, in order to dissolve the salt of the tertiary amine that has formed. The reaction product is isolated by shaking it with a solvent immiscible with water. It is, however, also possible to dilute the alcoholic reaction solution immediately after cooling by means of water until no further precipitation occurs and then to work up the reaction product as described above.

The alkylation with the aid of the esters of a hydrohalic acid or sulphonic acid may also be carried out without using a solvent, by merely heating the reactants to temperatures between 80 and 130°C. In order to bind the liberated acid the amine is advantageously used in an excess amount according to this method of operation.

As oxo - compounds of the formula IV used in the reduction in the presence of amines of the formula II, there may be mentioned saturated or unsaturated aldehydes or aliphatic ketones. When using unsaturated aldehydes, for example crotonaldehyde, its double linkage is also hydrogenated during the reaction. The reaction can be carried out in one or two reaction stages. An appropriate way of carrying out this method is to prepare first the corresponding alkylidene compound from the reaction components, to isolate this alkylidene compound and to hydrogenate it in a second stage. It is, however, also possible to omit the isolation of the intermediate product and to proceed in such a way that the amine of the formula II and the oxo - compound (aldehyde or ketone) in an equimolar ratio are

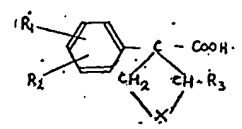
subjected to catalytic hydrogenation, advantageously in the presence of a solvent. If ketones are used as reaction components, an excess amount of ketone can be used which simultaneously serves as solvent. An excess amount of ketone does not affect the reaction, because ketone are not attacked by catalytic hydrogenation with noble metals. As catalysts there may be used, for example, metals of the 8th group of the Periodic System, particularly platinum, palladium, nickel and cobalt. When operating with noble metals as catalysts, temperatures of 40—50°C and a low hydrogen pressure have been found to be suitable. If base metals are used, it is advisable to employ temperatures between 80 and 120°C and a hydrogen pressure between 30 and 100 atmospheres gauge. The reaction mixture is worked up in the usual manner.

Another method of preparing the new compounds of the invention is by the reaction of amines of the formula II with alcohols of the Formula V in the presence of an excess amount of Raney nickel. In this method, the reactants are preferably heated for several hours to temperatures between 80 and 120°C, the alcohol advantageously being used in an excess amount. The reaction mixture is worked up in the usual manner by distilling off the excess solvent or by converting the reaction product into its hydrochloride.

According to another method of preparing the compounds of the invention it is also possible to start from carboxylic acid amides of the formula X and to reduce these compounds by means of lithium - aluminium hydride in ether. The carboxylic acid amides used as starting materials are advantageously prepared by reaction of the corresponding carboxylic acid halides with amines of the formula XII.

A further method of preparing the products according to the invention consists in the reduction of aldehydes of the formula XI in the presence of amines of the formula XII. The reaction is preferably carried out catalytically in the presence of organic solvents miscible with water, such as alcohols, dioxan or tetrahydrofuran. As catalysts there may be used, for example, metals of the 8th group of the Periodic System, for example nickel, cobalt, palladium or platinum. When using noble metal catalysts it is possible to effect the reaction only under a slight hydrogen pressure and at room temperature. If base metals are used it is advisable to operate at elevated temperatures and under an elevated gauge pressure of hydrogen.

To prepare the compounds of the invention, it is also possible to start from halides of the formula XIII and to react these compounds with amines of the formula XII, preferably in an inert organic solvent such as toluene or xylene at temperatures between 100 to 150°C. The starting materials are preferably prepared, for example, by reduction of corresponding carboxylic acids of the formula



with lithium - aluminium hydride and treatment of the alcohols so obtained with concentrated hydrobromic acid at an elevated temperature.

Furthermore, the compounds of the invention may be prepared by reacting compounds of the formula VI with amines of the formula II, it being preferable to operate in the presence of an appropriate organic solvent and an agent splitting off hydrogen halide. As solvents there are suitable compounds that are not miscible with water, for example toluene, benzene or xylene. The reaction is advantageously carried out at temperatures between 80 and 130°C and in the presence of agents binding inorganic acid, for example sodium carbonate or sodium bicarbonate. The reaction period depends upon the reactivity of the halogen compounds. It is of advantage to allow the starting material to continue reacting until the halogen in the reaction solution is only feebly detectable. The aforesaid method is particularly suitable if products are to be synthesized in the formula of which the symbols R_4 and R_5 together with nitrogen atom represent a saturated heterocyclic ring.

According to a further method of preparing the compounds of the invention, the corresponding acylamines of the formula IX whose acyl radical may contain 1—4 carbon atoms may be converted by means of lithium-aluminium hydride into the desired products by heating in an inert solvent. As inert solvent ether is, for example, suitable. The acyl compounds used as starting materials are obtained, for example, by treating primary amines of the formula II with acylating agents, for example acid halides or acid anhydrides. It is also possible to heat the primary amines of the formula II with corresponding aliphatic carboxylic acids in the presence of an anhydrous solvent, whereby water is split off.

Finally, the compounds according to the invention may be prepared by reacting amines of the formula VII with esters of the formula VIII. As esters of the formula VIII there may be mentioned, for example, alkylbromides or dialkyl sulphates. It is of advantage to heat the reactants, if necessary in the presence of an appropriate organic solvent.

The alkylation method according to Decker is most advantageously applied for preparing the compounds according to the invention. This method consists in reacting amines of the formula II with benzaldehyde and adding to

the benzylidene compound so obtained an ester of the formula III. From the addition product obtained the acid radical is subsequently split off by hydrolysis. It is of advantage to heat the benzylidene compound of the amine with an excess amount of the ester for several hours at 100°C, and then to add water to the reaction mixture and to separate by distillation with steam the benzaldehyde obtained as by-product. Sodium hydroxide solution is added to the remaining aqueous solution, the organic base is dissolved in an appropriate solvent and worked up as usual. As already mentioned, there may be used as esters of the formula III, for example, hydrohalic or sulphonic acid esters of aliphatic alcohols, especially dialkylsulphates.

The desired products may be synthesized also by heating amines of the formula II with dialkylsulphates, with formaldehyde and formic acid or with formaldehyde and hydrogen in the presence of hydrogenation catalysts, for example metals of the 8th group of the Periodic System, preferably nickel or palladium.

If the reaction products contain methoxy groups in their benzene nucleus, these may be demethylated according to a known method. A suitable method consists in heating the methoxy derivatives in a pressure vessel with concentrated hydrochloric acid or heating them at the boil for a prolonged period with hydrobromic acid of 48% strength or with pyridine hydrochloride.

By treating the products obtainable as described above with inorganic or organic acids they can be converted into the corresponding acid addition salts. For the salt formation there may be used, for example: inorganic acids such as hydrohalic acids, particularly hydrochloric and hydrobromic acid, or sulphuric acid, phosphoric acid or amidosulphonic acid.

As organic acids there enter into consideration, for example, acetic acid, propionic acid, oxalic acid, malic acid, succinic acid, lactic acid, maleic acid, fumaric acid, sorbic acid, citric acid, aceturic acid, aspartic acid, *p*-aminobenzoic acid, salicylic acid and ethylenediaminotetracetic acid.

While being well tolerated the compounds of the present invention are distinguished particularly by valuable central-analeptic properties. Based on numerically defined pharmacological comparitive tests the following Table shows the toxicity and pharmacological effects of a number of compounds of the present invention.

TABLE

No.	Compound	toxicity ($\sim LD_{50}$) in mice intravenously mg/kg	motility in mice treated with paraldehyde 100% = control subcutaneously 10 mg/kg	20 mg/kg
1	1-phenyl-1-sec.-butyl-aminomethylcyclopropane	40	300%	400%
2	1-phenyl-1-sec.-butyl-aminomethylcyclobutane	20	250%	350%
3	1-(3^1,4^1-dimethylphenyl) 1-sec.-butylaminomethyl-cyclopentane	20	250%	350%
4	1-(3^1,4^1-methylenedioxy-phenyl)-1-diethylamino-methylcyclopentane	30	300%	350%
5	1-(3^1-methoxy-phenyl)-1-diethylaminomethyl-cyclopentane	25	350%	400%

The compounds were examined as a motility in the paraldehyde mouse in Swiss albino mice having an average weight of 20 grams according to the test method published by L. Ther in "Süddeutsche Apothekerzeitung" 1953, pages 292—294, the following test conditions having been chosen:

In each case, three animals were placed for observation in glass cylinder and treated with paraldehyde. To each mouse there were given 600 milligrams/kilogram of body weight of paraldehyde by subcutaneous injection. 15 Minutes after this preliminary treatment the preparation being tested was also administered

subcutaneously. The tests were carried out in comparison with control animals pretreated with only paraldehyde. After a waiting period of 10 minutes the measurements of results was performed by recording each minute of an observation period of 1 hour whether and how many animals of the test group moved. The figures obtained by the observation of the non-treated control animals were designated at "motility of the paraldehyde controls" and their value was taken as 100. The increase in motility of the treated test groups as compared with the untreated controls was expressed as a percentage and the approximate value is shown in the Table.

It can be clearly deduced from the test results shown in the Table that the products of the present invention are very well tolerated and cause a considerable increase in motility even when administered in small doses. The results of the tests are all the more conclusive about the valuable properties of the compounds because their tolerance is much higher when subcutaneously administered than with intravenous administration. The toxicity figures shown in the Table correspond to the LD_{50} value ascertained by orientating examination upon intravenous application.

The products of the present invention are orally as well as parentally effective. Therefore, they can be used in admixture with suitable solid or liquid pharmaceutical carriers such as water, vegetable oils, starch, lactose, talc or auxiliary agents such as stabilizers, preserving, wetting or emulsifying agents, in the form of tablets, dragees, capsules, solutions, suspensions or emulsions. The products are preferably given *per os* in the form of tablets. They are preferably administered in a dose of 10—100 milligrams.

The following Examples illustrate the invention:

EXAMPLE 1

a) 1 - Phenyl - 1 - aminomethyl - cyclopropane

92 Grams of 1 - phenyl - 1 - cyano - cyclopropane are hydrogenated in 250 cc of methanol at 60—80°C while Raney nickel is used as catalyst. When the absorption of hydrogen has been terminated and the reaction mixture has been cooled, it is separated from the catalyst, the methanol is distilled off, the residue is dissolved in benzene and the benzenic solution is shaken with dilute hydrochloric acid. Nitrile that has not been hydrogenated remains dissolved in the benzene and can be recovered. The acid solution is separated off and the base is separated threfrom by means of dilute sodium hydroxide solution. After having been dissolved in benzene and after separation of the aqueous phase the benzene is distilled off and the remaining 1-phenyl - 1 - aminomethyl - cyclopropane is distilled under reduced pressure. Boiling point 98—102°C under a pressure of 12 mm of mercury. The yield amounts to 72 grams. The hydrochloride of the base melts at 175°C.

b) 1 - Phenyl - 1 - sec.-butylaminomethyl - cyclopropane

10 Grams of 1 - phenyl - 1 - aminomethyl - cyclopropane are hydrogenated under a hydrogen pressure of 50 atmospheres in 100 grams of methyl - ethyl - ketone at 50°C with palladium as catalyst until the absorption of hydrogen has been terminated. The reaction mixture is separated from the catalyst and after elimination by distillation of the excess methyl - ethyl - ketone the 1 - phenyl - 1 - sec. - butylaminomethyl - cyclopropane is obtained in a quantitative yield, forming a hydrochloride of a melting point of 97°C.

c) 1 - Phenyl - 1 - pyrrolidinomethyl - cyclopropane

20 Grams of 1 - phenyl - 1 - aminomethyl - cyclopropane are heated for 15 hours under reflux and while thoroughly stirring in 250 cc of xylene with 29.5 grams of 1,4 dibromobutane and 34 grams of anhydrous sodium carbonate. After termination of the heating the mixture is cooled, inorganic salts are filtered off with suction and the xylene is eliminated by distillation under reduced pressure. There remain behind 23 grams of crude 1 - phenyl - 1 - pyrrolidinomethyl - cyclopropane forming a hydrochloride of a melting point of 170°C.

EXAMPLE 2

a) 1 - Phenyl - 1 - aminomethyl - cyclobutane

As described in Example 1 a), 89 grams of 1 - phenyl - 1 - cyano - cyclobutane are hydrogenated and worked up. There are obtained 79 grams of crude 1 - phenyl - 1 - aminomethyl - cyclobutane which is purified by distillation under reduced pressure. Boiling point 115—117°C under a pressure of 10 mm of mercury.

b) 1 - Phenyl - 1 - sec.-butylaminomethyl - cyclobutane

In a manner analogous to that described in Example 1 b), there is obtained 1 - phenyl - 1 - sec. - butylaminomethyl - cyclobutane from 1 - phenyl - 1 - aminomethyl - cyclobutane by hydrogenation with methyl - ethyl - ketone and with the use of palladium as catalyst. The hydrochloride of the compound obtained melts at 113°C.

c) 1 - Phenyl - 1 - ethylaminomethyl - cyclobutane

24 grams of 1 - phenyl - 1 - aminomethyl - cyclobutane are heated for 5 hours at 100°C with 23.1 grams of diethyl - sulphate. After termination of the heating, water is added to the reaction mixture, the base is precipitated by means of sodium hydroxide solution, the precipitate is dissolved in ether and after drying and distilling off the ether 28 grams of 1 -

phenyl - 1 - ethylamino - methyl - cyclobutane are obtained. The hydrochloride of this compound melts at 166°C.

EXAMPLE 3

a) 1 - (3¹ - Methoxy - phenyl) - 1 - aminomethyl - cyclobutane

As described in Example 1 a), there are obtained from 294 grams of 1 - (3¹ - methoxy - phenyl) - 1 - cyano - cyclobutane by hydrogenation 249 grams of 1 - (3¹ - methoxy - phenyl) - 1 - aminomethyl - cyclobutane boiling at 120°C under a pressure of 3 mm of mercury. The hydrochloride melts at 128°C.

b) 1 - (3¹ - Methoxy - phenyl) - 1 - ethylaminomethyl - cyclobutane

As described in Example 2 c), 76.4 grams of 1 - (3¹ - methoxy - phenyl) - 1 - aminomethyl - cyclobutane are reacted with 61.6 grams of diethyl - sulphate and worked up. There are obtained 84 grams of 1 - (3¹ - methoxy - phenyl) - 1 - ethylaminomethyl - cyclobutane forming a hydrochloride of a melting point of 132°C.

c) 1 - (3¹ - Methoxy - phenyl) - 1 - diethylaminomethyl - cyclobutane

By the reaction of 44 grams of 1 - (3¹ - methoxy - phenyl) - 1 - ethylamino - methyl - cyclobutane with 31 grams of diethylsulphate there are obtained 44 grams of 1 - (3¹ - methoxy - phenyl) - 1 - diethylaminomethyl - cyclobutane, the hydrochloride of which melts at 160°C.

d) 1 - (3¹ - Methoxy - phenyl) - 1 - sec. - butylaminomethyl - cyclobutane

As described in Example 1 b), there is obtained by hydrogenation of 1 - (3¹ - methoxy - phenyl) - 1 - aminomethyl - cyclobutane with methyl - ethyl - ketone 1 - (3¹ - methoxy - phenyl) - 1 - sec. - butylaminomethyl - cyclobutane. The hydrochloride melts at 109°C.

e) 1 - (3¹ - Methoxy - phenyl) - 1 - pyrrolidino - methyl - cyclobutane

By the reaction of 1 - (3¹ - methoxy - phenyl) - 1 - aminomethyl - cyclobutane with 1,4 - dibromo - butane in a manner analogous to that described in Example 1 c) there is formed 1 - (3¹ - methoxy - phenyl) - 1 - pyrrolidinomethyl - cyclobutane whose hydrochloride melts at 185°C.

By heating for 8 hours under reflux the methoxy - phenyl compounds described in Examples 3 b), c), d) and e) with hydrobromic acid of 48% strength the methyl group is split off while the corresponding hydroxy - phenyl derivatives are formed. The following products were prepared:

1 - (3¹ - hydroxy - phenyl) - 1 - ethylaminomethyl - cyclobutane, melting point of the hydrochloride 166°C;

1 - (3¹ - hydroxy - phenyl) - 1 - diethylaminomethyl - cyclobutane, melting point of the hydrochloride 162°C;

1 - (3¹ - hydroxy - phenyl) - 1 - sec. - butylaminomethyl - cyclobutane, melting point of the hydrochloride 142°C;

1 - (3¹ - hydroxy - phenyl) - 1 - pyrrolidinomethyl - cyclobutane, melting point of the hydrochloride 182°C.

The 1 - (3¹ - methoxy - phenyl) - 1 - cyano - cyclobutane showing a boiling point of 136—138°C under a pressure of 3 mm of mercury, used as starting material, is obtained by the reaction of 3 - methoxy - benzyl - cyanide with 2 mols of sodium amide and 1 mol of 1,3 - dibromopropane at 30—35°C.

EXAMPLE 4

a) 1 - Phenyl - 1 - aminomethyl - cyclopentane

As described in Example 1 a), there are obtained by hydrogenation when starting from 148 grams of 1 - phenyl - 1 - cyano - cyclopentane 132 grams of 1 - phenyl - 1 - aminomethyl - cyclopentane boiling at 130—132°C under a pressure of 10 mm of mercury.

b) 1 - Phenyl - 1 - dimethylaminomethyl - cyclopentane

87 grams of 1 - phenyl - 1 - aminomethyl-cyclopentane are heated for 3 hours on a steam bath with 92 grams of formic acid and 150 grams of formaldehyde of 30% strength. After cooling, sodium hydroxide solution is added to the mixture, the latter is extracted with ether and after drying and distilling off the ether, 90 grams of 1 - phenyl - 1 - dimethylaminomethyl - cyclopentane are obtained. The hydrochloride of the substance melts at 230°C.

The same compound is obtained by hydrogenation at room temperature of 1 - phenyl - 1 - amino - methyl - cyclopentane with formaldehyde and hydrogen in the presence of palladium as catalyst.

c) 1 - Phenyl - 1 - ethylaminomethyl - cyclopentane

In a manner analogous to that described in Example 2 c), there is obtained from 1 - phenyl - 1 - aminomethyl - cyclopentane by reaction with diethyl - sulphate 1 - phenyl - 1 - ethylaminomethyl - cyclopentane. The hydrochloride of the compound melts at 178°C. The same compound is obtained by catalytic hydrogenation of 1 - phenyl - cyclopentane - 1 - aldehyde in the presence of ethylamine. The above-mentioned 1 - phenyl - cyclopentane - 1 - aldehyde is preferably synthesized by heating 1 - phenyl - 1 - hydroxymethyl - cyclopentane with selenium - dioxide in an inert solvent.

d) 1 - Phenyl - 1 - diethylaminomethyl - cyclopentane

In a manner analogous to that described in Example 3 c), there is obtained from 1 -

phenyl - 1 - ethylaminomethyl - cyclopentane 1 - phenyl - 1 - diethylaminomethyl - cyclopentane. The hydrochloride of the compound melts at 165°C.

The same compound is obtained by reducing 1 - phenyl - cyclopentane - 1 - carboxylic acid diethylamide with lithium - aluminium - hydride or by reacting 1 - phenyl - 1 - bromomethyl - cyclopentane at about 150°C with diethylamine.

The 1 - phenyl - 1 - bromomethyl - cyclopentane used as starting material can be prepared as follows: 1 - phenyl - cyclopentane - 1 - carboxylic acid is reduced with lithium - aluminium - hydride in an ethereal solution, whereby 1 - phenyl - 1 - hydroxymethyl - cyclopentane is formed which melts at 46°C. When heating the latter compound with concentrated hydrobromic acid 1 - phenyl - 1 - bromomethyl - cyclopentane is formed. 1 - Phenyl - cyclopentane - 1 - carboxylic acid is obtained, for example, by the hydrolysis of 1 - phenyl - 1 - cyano - cyclopentane.

EXAMPLE 5

a) 1 - (4^1 - Methyl - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained by hydrogenation from 50 grams of 1 - (4^1 - methyl - phenyl) - 1 - cyano - cyclopentane 42 grams of 1 - (4^1 - methyl - phenyl) - 1 - amino - methyl - cyclopentane boiling at 146—148°C under a pressure of 12 mm of mercury.

b) 1 - (4^1 - methyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane

In a manner analogous to that described in Example 1 b), there is obtained by hydrogenation of 1 - (4^1 - methyl - phenyl) - 1 - amino - methyl - cyclopentane with methyl - ethyl - ketone and palladium as catalyst 1 - (4^1 - methyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane whose hydrochloride melts at 169°C.

The 1 - (4^1 - methyl - phenyl) - 1 - cyano - cyclopentane used as starting material and boiling at 158—160°C under a pressure of 12 mm of mercury can be obtained by the reaction of 1 mol of 4 - methyl - benzyl - cyanide with 2 mols of sodium - amide and 1 mol of 1,4 - dibromo - butane in benzene at 50—60°C.

EXAMPLE 6

a) 1 - (2^1,4^1 - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained from 42 grams of 1 - (2^1,4^1 - dimethyl - phenyl) - 1 - cyano - cyclopentane by hydrogenation 41 grams of 1 - (2^1,4^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane from which a hydrochloride melting at 183°C is obtained.

b) 1 - (2^1,4^1 - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane

In a manner analogous to that described in Example 1 b), there is obtained by hydrogenation of 1 - (2^1,4^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane with methyl - ethyl - ketone 1 - (2^1,4^1 - dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane which forms a hydrochloride melting at 201°C.

The 1 - (2^1,4^1 - dimethyl - phenyl) - 1 - cyano - cyclopentane used as starting material and boiling at 146—148°C under a pressure of 4 mm of mercury can be prepared by the reaction of 2,4 - dimethyl - benzyl - cyanide with 2 mols of sodium - amide and 1 mol of 1,4 - dibromobutane in benzene at 50—60°C.

EXAMPLE 7

a) 1 - (2^1,5^1 - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained from 50 grams of 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - cyano - cyclopentane by hydrogenation 45 g of 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - aminomethyl - pentane whose hydrochloride melts at 208°C.

b) 1 - (2^1,5^1 - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane

In a manner analogous to that described in Example 1 b), there is obtained by hydrogenation of 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - amino - methyl - cyclopentane with methyl - ethyl - ketone 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane. The hydrochloride melts at 181°C.

c) 1 - (2^1,5^1 - Dimethyl - phenyl) - 1 - allylaminomethyl - cyclopentane

25 Grams of 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane are dissolved in 60 cc of benzene and 7.5 grams of allylbromide are added. The mixture is boiled for 8 hours under reflux, cooled, the hydrobromide that has formed from the initial base is separated off and the benzene solution is washed with water. The solvent is distilled off. 13 Grams of 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - allylaminomethyl - cyclopentane are obtained. The hydrochloride melts at 143°C.

d) 1 - (2^1,5^1 - Dimethyl - phenyl) - 1 - cyano-cyclopentane

By the reaction of 2,5 - dimethyl - benzyl-cyanide with sodium - amide and 1,4 - dibromobutane 1 - (2^1,5^1 - dimethyl - phenyl) - 1 - cyano - cyclopentane is obtained in the usual manner. The substance boils at 144—146°C under a pressure of 4 mm of mercury.

EXAMPLE 8

a) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained from 66 grams of 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - cyano - cyclopentane by hydrogenation 60 grams of 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane boiling at 163—165°C under a pressure of 11 mm of mercury. The corresponding hydrochloride melts at 170°C.

b) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - dimethylaminomethyl - cyclopentane

According to the method indicated in Example 4 b), there is obtained by reaction of 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - amino - methyl - cyclopentane with formaldehyde and formic acid 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - dimethylaminomethyl - cyclopentane. Its hydrochloride melts at 252°C.

c) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - ethylaminomethyl - cyclopentane

In a manner analogous to that described in Example 2 c), there is obtained by reaction of 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - amino - methyl - cyclopentane with diethyl - sulphate 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - ethylaminomethyl - cyclopentane. Its hydrochloride melts at 138°C.

The same compound is obtained by treating N - acetyl - 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane in an ethereal solution with lithium - aluminium - hydride.

d) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - diethylaminomethyl - cyclopentane

According to the method described in Example 3 c), there is obtained from 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - diethylaminomethyl - cyclopentane. The hydrochloride of the compound melts at 147°C.

e) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - *n* - butylaminomethyl - cyclopentane

The above-mentioned product can be obtained by hydrogenation with *n* - butyraldehyde or by 15 hours' heating with an excess amount of *n* - butanol and a large amount of Raney nickel or by reduction of the corresponding *n* - butyryl compound with lithium - aluminium - hydride. The hydrochloride of the compound melts at 124°C. The hydrogenation with *n* - butyraldehyde is effected under the reaction conditions described in Example 1 b). Instead of with *n* - butyraldehyde the hydrogenation can also be carried out with crotonaldehyde.

f) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - isobutylaminomethyl - cyclopentane

Under the same reaction conditions as described in Example 1 b), there is obtained from 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane by hydrogenation with isobutyraldehyde 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - isobutylaminomethyl - cyclopentane. Its hydrochloride melts at 158°C.

g) By hydrogenation with acetone, methyl - ethyl - ketone, cyclo - pentanone and cyclohexanone the following compounds were prepared according to the method described in Example 1 b):

1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - isopropylaminomethyl - cyclopentane. Melting point of the hydrochloride 191°C.

1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane. Melting point of the hydrochloride 168°C.

1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - cyclopentylaminomethyl - cyclopentane. Melting point of the hydrochloride 172°C.

1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - cyclohexylaminomethyl - cyclopentane. Melting point of the hydrochloride 174°C.

h) 1 - (3¹,4¹ - Dimethyl - phenyl) - 1 - pyrrolidinomethyl - cyclopentane

According to the method described in Example 1 c), there is obtained by reaction of 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - aminomethyl - cyclopentane with 1,4 - dibromo - butane 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - pyrrolidinomethyl - cyclopentane whose hydrochloride melts at 211°C.

The 1 - (3¹,4¹ - dimethyl - phenyl) - 1 - cyano - cyclopentane (boiling point 154—157°C under a pressure of 4 mm of mercury) can be obtained by reaction of 3,4 - dimethyl - benzyl - cyanide with sodium - amide and 1,4 - dibromo - butane.

EXAMPLE 9

a) 1 - (3¹ - Methoxy - phenyl) - 1 - amino - methyl - cyclopentane

According to the method described in Example 1 a), there are obtained by hydrogenation of 60 grams of 1 - (3¹ - methoxy - phenyl) - 1 - cyano - cyclopentane 47 grams of 1 - (3¹ - methoxy - phenyl) - 1 - amino - methyl - cyclopentane boiling at 161—162°C under a pressure of 9 mm of mercury.

The following compounds were prepared from 1 - (3¹ - methoxy - phenyl) - 1 - amino - methyl - cyclopentane:

b) 1 - (3¹ - Methoxy - phenyl) - 1 - ethylaminomethyl - cyclopentane; melting point of the hydrochloride 138°C, obtained by re-

action with diethyl - sulphate in a manner analogous to that described in Example 2 c).

The reaction of 1 - (3¹ - methoxy - phenyl) - 1 - ethylaminomethyl - cyclopentane with diethyl - sulphate in an analogous manner to that described in Example 3 c) yields 1 - (3¹ - methoxy - phenyl) - 1 - diethylaminomethyl - cyclopentane whose hydrochloride melts at 98°C.

c) 1 - (3¹ - Methoxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane; melting point of the hydrochloride 204°C, obtained by reaction with 1,4 - dibromobutane in an analogous manner to that described in Example 1 c).

d) 1 - (3¹ - Methoxy - phenyl) - 1 - piperidinomethyl - cyclopentane; melting point of the hydrochloride 176°C, obtained by reaction with 1,5 - dibromopentane in an analogous manner to that described in Example 1 c).

By heating for 8 hours the methoxyphenyl compounds described in Examples 9 b), c) and d) with hydrobromic acid of 48% strength according to the method described in Example 3 the following products were obtained:

1 - (3¹ - Hydroxy - phenyl) - 1 - diethylaminomethyl - cyclopentane; melting point of the hydrochloride 175°C.

1 - (3¹ - Hydroxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane; melting point of the hydrochloride 146°C.

1 - (3¹ - Hydroxy - phenyl) - 1 - piperidinomethyl - cyclopentane; melting point of the hydrochloride 201°C.

The 1 - (3¹ - methoxy - phenyl) - 1 - cyanocyclopentane boiling at 186—188°C under a pressure of 20 mm of mercury was obtained by the reaction of 3 - methoxy - benzyl - cyanide with sodium amide and 1,4 - dibromobutane.

EXAMPLE 10

a) 1 - (3¹,4¹ - Dimethoxy - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained from 123 grams of 1 - (3¹,4¹ - dimethoxy - phenyl) - 1 - cyano - cyclopentane by hydrogenation 110 grams of 1 - (3¹,4¹ - dimethoxy - phenyl) - 1 - aminomethyl - cyclopentane boiling at 154—156°C under a pressure of 0.1 mm of mercury. The hydrochloride melts at 199°C.

From 1 - (3¹,4¹ - dimethoxy - phenyl) - 1 - aminomethyl - cyclopentane the following compounds were prepared:

b) 1 - (3¹,4¹ - Dimethoxy - phenyl) - 1 - ethylaminomethyl - cyclopentane; melting point of the hydrochloride 166°C; obtained by reaction with diethyl - sulphate in an analogous manner to that described in Example 2 c).

By the reaction of 1 - (3¹,4¹ - dimethoxyphenyl) - 1 - ethylaminomethyl - cyclopentane with diethyl - sulphate there was obtained 1 - (3¹,4¹ - dimethoxy - phenyl) - 1 - diethylaminomethyl - cyclopentane by a method analogous to that described in Example 3 c). The hydrochloride of the substance melts at 161°C.

c) 1 - (3¹,4¹ - Dimethoxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane. Melting point of the hydrochloride: 206°C; obtained by reaction with 1,4 - dibromo - butane in a manner analogous to that described in Example 1 c).

1 - (3¹,4¹ - Dimethoxy - phenyl) - 1 - cyano - cyclopentane boiling at 178—180°C under a pressure of 0.1 mm of mercury was obtained by reaction of 3,4 - dimethoxy - benzylcyanide with sodium amide and 1,4 - dibromo - butane.

EXAMPLE 11

a) 1 - (3¹,4¹ - Methylene - dioxy - phenyl) - 1 - aminomethyl - cyclopentane

According to the method described in Example 1 a), there are obtained by hydrogenation of 140 grams of 1 - (3¹,4¹ - methylene-dioxy - phenyl) - 1 - cyano - cyclopentane 125 grams of 1 - (3¹,4¹ - methylene - dioxy - phenyl) - 1 - aminomethyl - cyclopentane melting at 60°C.

b) 1 - (3¹,4¹ - Methylene - dioxy - phenyl) - 1 - methylaminomethyl - cyclopentane

18 Grams of benzaldehyde are added to 33 grams of the base in 100 cc of methanol and the reaction mixture is heated on a steam bath for 30 minutes. After cooling, the benzylidene compound formed precipitates, it is filtered off with suction and washed with cold methanol. The yield amounts to 41 grams; melting point: 59°C.

41 Grams of the benzylidene compound are heated for 5 hours at 100°C with 35 grams of dimethyl - sulphate. After termination of the heating water is added to the mixture and the benzaldehyde set free in the course of the reaction is eliminated by distillation with steam. From the remaining aqueous solution the base is precipitated by means of sodium hydroxide solution, the precipitate is dissolved in ether and after drying and distilling off the solvent there are obtained 27 grams of 1 - (3¹,4¹ - methylene - dioxy - phenyl) - methylaminomethyl - cyclopentane whose hydrochloride melts at 250°C.

From 1 - (3¹,4¹ - methylene - dioxy - phenyl) - 1 - aminomethyl - cyclopentane the following compounds were likewise obtained:

c) 1 - (3¹,4¹ - Methylene - dioxy - phenyl) - 1 - ethylaminomethyl - cyclopentane; melting point of the hydrochloride: 174°C, obtained by treatment with diethyl - sulphate according to the method of Example 2 c). The reaction of the monoethylamino compound with diethyl - sulphate according to a method analogous to that described in Example 3 c) produced 1 - (3¹,4¹ - methylene - dioxy - phenyl) - 1 - diethylamino - methyl - cyclopentane. Melting point of the hydrochloride: 146°C.

d) 1 - (3¹,4¹ - Methylene - dioxy - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane;

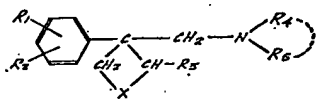
melting point of the hydrochloride: 184°C, obtained by hydrogenation with methyl - ethyl - ketone in a manner analogous to that described in Example 1 b).

e) 1 - (3¹,4¹ - Methylene - dioxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane; melting point of the hydrochloride: 228°C, obtained by reaction with 1,4 - dibromo - butane in a manner analogous to that described in Example 1 c).

The 1 - (3¹,4¹ - methylene - dioxy - phenyl) - 1 - cyano - cyclopentane boiling at 158—160°C under a pressure of 2 mm of mercury was obtained by the reaction of 3,4 - methylene - dioxy - benzylcyanide with sodium amide and 1,4 - dibromo - butane.

WHAT WE CLAIM IS:—

1. A phenyl - cycloalkane - methylamine of the formula I



I

in which R_1 and R_2 each represents a hydrogen atom or a hydroxy, methyl or methoxy group, or together represent a methylenedioxy group, X together with the CH_2 and CHR_3 groups and the adjacent carbon atom represent a cycloalkane ring containing 3 to 5 carbon atoms, R_3 represents a hydrogen atom or an alkyl group containing 1 to 3 carbon atoms, R_4 and R_5 each represents a hydrogen atom, a saturated or unsaturated aliphatic hydrocarbon group containing up to 4 carbon atoms or a cycloalkyl group containing 4 to 6 carbon atoms or together with the nitrogen atom represent a saturated ring which may be interrupted by a further hetero atom.

2. An acid addition salt of a compound as claimed in claim 1.

3. A physiologically tolerable acid addition salt of a compound as claimed in claim 1.

4. 1 - Phenyl - 1 - aminomethyl - cyclopropane.

5. 1 - Phenyl - 1 - sec. - butylaminomethyl - cyclopropane.

6. 1 - Phenyl - 1 - pyrrolidinomethyl - cyclopropane.

7. 1 - Phenyl - 1 - aminomethyl - cyclobutane.

8. 1 - Phenyl - 1 - sec. - butylaminomethyl - cyclobutane.

9. 1 - Phenyl - 1 - ethylaminomethyl - cyclobutane.

10. 1 - (3¹ - Methoxy - phenyl) - 1 - aminomethyl - cyclobutane.

11. 1 - (3¹ - Methoxy - phenyl) - 1 - ethylaminomethyl - cyclobutane.

12. 1 - (3¹ - Methoxy - phenyl) - 1 - diethylaminomethyl - cyclobutane.

13. 1 - (3¹ - Methoxy - phenyl) - 1 - sec. - butylaminomethyl - cyclobutane.

14. 1 - (3¹ - Methoxy - phenyl) - 1 - pyrrolidino - methyl - cyclobutane.

15. 1 - (3¹ - Hydroxy - phenyl) - 1 - ethylaminomethyl - cyclobutane.

16. 1 - (3¹ - Hydroxy - phenyl) - 1 - diethylaminomethyl - cyclobutane.

17. 1 - (3¹ - Hydroxy - phenyl) - 1 - sec. - butylaminomethyl - cyclobutane.

18. 1 - (3¹ - Hydroxy - phenyl) - 1 - pyrrolidinomethyl - cyclobutane.

19. 1 - Phenyl - 1 - aminomethyl - cyclopentane.

20. 1 - Phenyl - 1 - dimethylaminomethyl - cyclopentane.

21. 1 - Phenyl - 1 - ethylaminomethyl - cyclopentane.

22. 1 - Phenyl - 1 - diethylaminomethyl - cyclopentane.

23. 1 - (4¹ - Methyl - phenyl) - 1 - aminomethyl - cyclopentane.

24. 1 - (4¹ - Methyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane.

25. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane.

26. 1 - (2¹:4¹ - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane.

27. 1 - (2¹:5¹ - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane.

28. 1 - (2¹:5¹ - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane.

29. 1 - (2¹:5¹ - Dimethyl - phenyl) - 1 - allylaminomethyl - cyclopentane.

30. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - aminomethyl - cyclopentane.

31. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - dimethylaminomethyl - cyclopentane.

32. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - ethylaminomethyl - cyclopentane.

33. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - diethylaminomethyl - cyclopentane.

34. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - *n* - butylaminomethyl - cyclopentane.

35. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - isobutylaminomethyl - cyclopentane.

36. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - isopropylaminomethyl - cyclopentane.

37. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane.

38. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - cyclopentylaminomethyl - cyclopentane.

39. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - cyclohexylaminomethyl - cyclopentane.

40. 1 - (3¹:4¹ - Dimethyl - phenyl) - 1 - pyrrolidinomethyl - cyclopentane.

41. 1 - (3¹ - Methoxy - phenyl) - 1 - aminomethyl - cyclopentane.

42. 1 - (3¹ - Methoxy - phenyl) - 1 - ethylaminomethyl - cyclopentane.

43. 1 - (3¹ - Methoxy - phenyl) - 1 - diethylaminomethyl - cyclopentane.

44. 1 - (3¹ - Methoxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane.

45. 1 - (3¹ - Methoxy - phenyl) - 1 - piperidinomethyl - cyclopentane.
46. 1 - (3¹ - Hydroxy - phenyl) - 1 - diethylaminomethyl - cyclopentane.
47. 1 - (3¹ - Hydroxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane.
48. 1 - (3¹ - Hydroxy - phenyl) - 1 - piperidinomethyl - cyclopentane.
49. 1 - (3¹:4¹ - Dimethoxy - phenyl) - 1 - aminomethyl - cyclopentane.
50. 1 - (3¹:4¹ - Dimethoxy - phenyl) - 1 - ethylaminomethyl - cyclopentane.
51. 1 - (3¹:4¹ - Dimethoxy - phenyl) - 1 - diethylaminomethyl - cyclopentane.
52. 1 - (3¹:4¹ - Dimethoxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane.
53. 1 - (3¹:4¹ - Methylene - dioxy - phenyl) - 1 - aminomethyl - cyclopentane.
54. 1 - (3¹:4¹ - Methylenedioxy - phenyl) - 1 - methylaminomethyl - cyclopentane.
55. 1 - (3¹:4¹ - Methylenedioxy - phenyl) - 1 - ethylaminomethyl - cyclopentane.
56. 1 - (3¹:4¹ - Methylenedioxy - phenyl) - 1 - diethylaminomethyl - cyclopentane.
57. 1 - (3¹:4¹ - Methylenedioxy - phenyl) - 1 - sec. - butylaminomethyl - cyclopentane.
58. 1 - (3¹:4¹ - Methylenedioxy - phenyl) - 1 - pyrrolidinomethyl - cyclopentane.
59. A physiologically tolerable acid addition salt of the compound claimed in any one of claims 4 to 58.
60. The hydrochloride of the compound claimed in any one of claims 4 to 58.
61. A pharmaceutical preparation which comprises a compound as claimed in claim 1, in admixture or conjunction with a pharmaceutically suitable carrier.
62. A pharmaceutical preparation which comprises a physiologically tolerable acid addition salt as claimed in claim 3 in admixture or conjunction with a pharmaceutically suitable carrier.
63. A pharmaceutical preparation which comprises the compound claimed in any one of claims 4 to 58 in admixture or conjunction with a pharmaceutically suitable carrier.
64. A pharmaceutical preparation which comprises a physiologically tolerable salt as claimed in claim 59 to 60 in admixture or conjunction with a pharmaceutically suitable carrier.
65. A process for the manufacture of a phenyl - cycloalkane - methylamine, conducted substantially as described in any one of the Examples herein.

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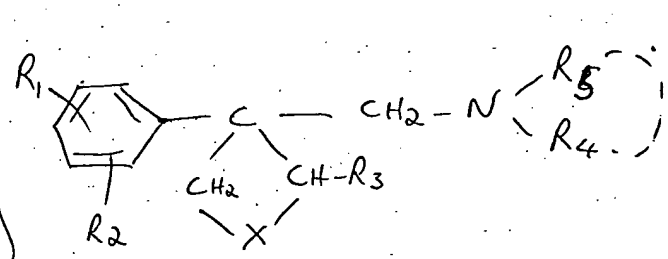

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X = residue of cyclo-alkane ring